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26. (amended) The cell transduction vector of claim 25, wherein the vector is pBAR-EDN.

REMARKS

With entry of the instant amendment, claims 1, 2, 14, 20, and 26 have been amended and claims 3 and 29 have been canceled. Accordingly, claims 1, 2, 4-28, and 30-35, 37, 38, and 40-42 are pending in the application. A copy of the pending claims is provided in Appendix B.

The amendments to the claims add no new matter and are supported throughout the specification and claims as filed.

Claim 1 has been amended to recite an HIV packaging site; claim 14 has been amended to recite an HIV retroviral particle. Support for the amendment can be found in the application, for example, on page 21, line 15 through page 22, line 6.

Claims 1 and 2 have been amended to recite an HIV Rev binding subsequence. Support for the amendment can be found in the application, for example, on page 9, lines 4-17 and claim 3 as filed.

The rejections are addressed in the order presented in the Office Action mailed November 8, 2001.

*Rejections under 35 U.S.C. § 112, first paragraph*

Claim 1-35, 41, and 42

Claims 1-35, 41, and 42 stand rejected as allegedly not enabled. The rejection alleges that it is unpredictable to combine several sub-sequences in tandem without direction in the specification as to what parts of the entire sequence would or would not work. Applicants disagree with the Examiner for reasons of record. However, in order to expedite prosecution, Applicants have amended the claims to recite specific HIV elements, which elements provide an HIV backbone.

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The Advisory Action mailed June 4 indicated that the amendment to the claims to recite an HIV-based cell transduction vector overcomes this issue. Applicants therefore respectfully request withdrawal of the rejection.

Claims 20 and 26

Claims 20 and 26 stand rejected as allegedly not enabled for conservative modifications of the aforementioned vectors. In order to expedite prosecution, the claims as amended. Applicants therefore respectfully request withdrawal of the rejection.

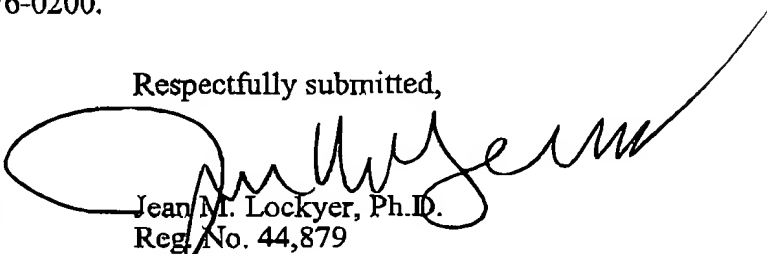
Claim 29

In order to expedite prosecution, claim 29 has been cancelled. Applicants therefore respectfully request withdrawal of the rejection as applied to claim 29.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is urged. If the Examiner believes a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at 415-576-0200.

Respectfully submitted,



Jean M. Lockyer, Ph.D.  
Reg. No. 44,879

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, 8<sup>th</sup> Floor  
San Francisco, California 94111-3834  
Tel: (415) 576-0200  
Fax: (415) 576-0300  
JML  
SF 1383231 v1

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**APPENDIX A**  
**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (amended) An HIV-based cell transduction vector comprising a vector nucleic acid encoding:

[a retroviral] an HIV packaging site;  
a first viral inhibitor subsequence;  
a splice donor site subsequence;  
a splice acceptor site subsequence;  
[a retroviral] an HIV Rev binding subsequence; and,  
a promoter subsequence;

wherein:

the first viral inhibitor subsequence is located between the splice donor site subsequence and the splice acceptor site subsequence;

the splice donor site subsequence and the splice acceptor site subsequence permit splicing of the first viral inhibitor subsequence from the vector nucleic acid in the nucleus of a cell; and,

the promoter subsequence is operably linked to the first viral inhibitor subsequence.

2. (amended) The cell transduction vector of claim 1, wherein the vector nucleic acid further encodes [a retroviral] an HIV Rev binding subsequence, wherein the vector nucleic acid is translocated to the cytoplasm in the presence of [a] an HIV Rev protein, and wherein splicing of the first viral inhibitor sequence is inhibited by Rev.

14. (amended) The cell transduction vector of claim 1, wherein the vector comprises [a] an HIV retroviral particle.

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20. (amended) The cell transduction vector of claim 1, wherein the cell transduction vector is selected from the group of cell transduction vectors consisting of pBAR, pBAR-ONC, and pBAR-EDN [and conservative modifications thereof].

26. (amended) The cell transduction vector of claim 25, wherein the vector is pBAR-EDN[, or a conservative modification thereof].

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**APPENDIX B**  
**CURRENTLY PENDING CLAIMS**

1. (amended) An HIV-based cell transduction vector comprising a vector nucleic acid encoding:
  - an HIV packaging site;
  - a first viral inhibitor subsequence;
  - a splice donor site subsequence;
  - a splice acceptor site subsequence;
  - an HIV Rev binding subsequence; and,
  - a promoter subsequence;wherein:
  - the first viral inhibitor subsequence is located between the splice donor site subsequence and the splice acceptor site subsequence;
  - the splice donor site subsequence and the splice acceptor site subsequence permit splicing of the first viral inhibitor subsequence from the vector nucleic acid in the nucleus of a cell; and,
  - the promoter subsequence is operably linked to the first viral inhibitor subsequence.
2. (amended) The cell transduction vector of claim 1, wherein the vector nucleic acid further encodes an HIV Rev binding subsequence, wherein the vector nucleic acid is translocated to the cytoplasm in the presence of an HIV Rev protein, and wherein splicing of the first viral inhibitor sequence is inhibited by Rev.
4. (as filed) The cell transduction vector of claim 1, wherein the first viral inhibitor comprises a nucleic acid subsequence encoding a ribonuclease selected from the pancreatic RNase A superfamily.

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5. (as filed) The cell transduction vector of claim 1, wherein the first viral inhibitor comprises a nucleic acid subsequence encoding a ribonuclease selected from the group of ribonucleases consisting of Onconase, modified Onconase, and EDN.

6. (as filed) The cell transduction vector of claim 1, wherein the first viral inhibitor subsequence encodes a transdominant protein selected from the group of transdominant proteins consisting of transdominant Gag, transdominant Tat, and transdominant Rev.

7. (as filed) The cell transduction vector of claim 1, wherein the vector further comprises a cell binding ligand selected from the group consisting of transferrin, *c-kit* ligand, an interleukin and a cytokine.

8. (as filed) The cell transduction vector of claim 1, wherein the promoter is selected from the group of promoters consisting of a retroviral LTR promoter, a constitutive promoter, an inducible promoter, a tissue specific promoter, a CMV promoter, a probasin promoter and a tetracycline-responsive promoter.

9. (as filed) The cell transduction vector of claim 1, wherein the vector further comprises an encephalomyocarditis virus internal ribosome entry site (IRES).

10. (as filed) The cell transduction vector of claim 1, wherein the vector nucleic acid further encodes a second viral inhibitor.

11. (amended) The cell transduction vector of claim 9, wherein the vector nucleic acid further encodes a second viral inhibitor, wherein expression of the second viral inhibitor is controlled by the IRES.

12. (as filed) The cell transduction vector of claim 1, wherein vector nucleic acid further encodes a multicistronic mRNA with a first open reading frame and a

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second open reading frame, which multicistronic mRNA comprises an IRES sequence which directs translation of the second open reading frame in a cell.

13. (as filed) The cell transduction vector of claim 11, wherein the first open reading frame encodes a viral inhibitor.

14. (amended) The cell transduction vector of claim 1, wherein the vector comprises an HIV retroviral particle.

15. (as filed) The cell transduction vector of claim 1, wherein the vector nucleic acid is packaged into an HIV particle in a cell infected by a wild-type HIV.

16. (as filed) The cell transduction vector of claim 1, wherein the vector nucleic acid is packaged in a liposome.

17. (as filed) The cell transduction vector of claim 14, wherein the retroviral particle is pseudotyped for transduction into hematopoietic stem cells.

18. (as filed) The cell transduction vector of claim 1, wherein the vector further comprises a pharmaceutical excipient.

19. (as filed) The cell transduction vector of claim 1, wherein the vector nucleic acid further encodes a reporter gene.

20. (amended) The cell transduction vector of claim 1, wherein the cell transduction vector is selected from the group of cell transduction vectors consisting of pBAR, pBAR-ONC, and pBAR-EDN.

21. (as filed) The cell transduction vector of claim 1, wherein the viral inhibitor is an oncogene inhibitor.

22. (as filed) The cell transduction vector of claim 1, wherein the vector further comprises an oncogene inhibitor.

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23. (as filed) The cell transduction vector of claim 22, wherein the oncogene inhibitor is a nucleic acid encoding an inhibitor selected from the group of inhibitors consisting of an antibody which specifically binds a Ras protein and an RNase.

24. (as filed) The cell transduction vector of claim 22, wherein the oncogene inhibitor is an RNase from the RNase A superfamily.

25. (as filed) A cell transduction vector comprising a nucleic acid subsequence encoding an EDN protein, which subsequence is operably linked to a promoter, wherein said cell transduction vector inhibits the replication of a retrovirus in a cell transduced by the cell transduction vector.

26. (amended) The cell transduction vector of claim 25, wherein the vector is pBAR-EDN.

27. (as filed) The cell transduction vector of claim 25, wherein the cell is a CD4<sup>+</sup> cell

28. (as filed) The cell transduction vector of claim 25, wherein the cell is a stem cell.

30. (as filed) The cell transduction vector of claim 25, wherein the vector nucleic acid is packaged in a retroviral particle.

31. (as filed) The cell transduction vector of claim 25, wherein the vector is packaged in a liposome.

32. The cell transduction vector of claim 25, wherein the vector comprises a cell binding ligand selected from the group of cell binding ligands consisting of transferrin, kit-ligand, an interleukin, and a cytokine.



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33. (as filed) The cell transduction vector of claim 25, wherein the vector nucleic acid further encodes a subsequence encoding a retroviral chromosome integration subsequence.

34. (as filed) The cell transduction vector of claim 25, wherein the vector further comprises a multicistronic mRNA which encodes a first open reading frame and a second open reading frame, which multicistronic mRNA is operably linked to a promoter, wherein the dicistronic mRNA comprises a subsequence encoding EDN.

35. (as filed) The cell transduction vector of claim 25, wherein the promoter is selected from the group consisting of a tetracycline responsive promoter, a probasin promoter, and a CMV promoter.

37. (amended) A method of transducing a cell with a nucleic acid encoding a viral inhibitor comprising contacting the cell with the cell transduction vector of claim 1, wherein the cell is transduced *in vitro*.

38. (amended) A method of inhibiting the growth of HIV in a cell comprising transducing the cell with the cell transduction vector of claim 1, wherein the cell is transduced *in vitro*.

40. (amended) The method of claim 38, wherein the cell is selected from the group of cells consisting of transferrin receptor<sup>+</sup> cells, CD4<sup>+</sup> cells and CD34<sup>+</sup> hematopoietic stem cells.

41. (as filed) A cell comprising the cell transduction vector of claim 1.

42. (as filed) The cell of claim 41, wherein the cell is selected from the group of cells comprising CD4<sup>+</sup> cells, CD34<sup>+</sup> hematopoietic stem cells, and transferrin receptor<sup>+</sup> cells.